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The Commissioner of Patents and Trademarks

10853 U.S. PTO
09/693213
10/19/00

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America for the term set forth below, subject to the payment of maintenance fees as provided by law.

If this application was filed prior to June 8, 1995, the term of this patent is the longer of seventeen years from the date of grant of this patent or twenty years from the earliest effective U.S. filing date of the application, subject to any statutory extension.

If this application was filed on or after June 8, 1995, the term of this patent is twenty years from the U.S. filing date, subject to any statutory extension. If the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121 or 365(c), the term of the patent is twenty years from the date on which the earliest application was filed, subject to any statutory extension.

Bruce Lehman

Commissioner of Patents and Trademarks

Pandra Morton

Attest

United States Patent [19]

Petrie et al.



US005824796A

[11] Patent Number: 5,824,796

[45] Date of Patent: Oct. 20, 1998

[54] CROSS-LINKING OLIGONUCLEOTIDES

[75] Inventors: Charles R. Petrie; Rich B. Meyer.
both of Woodinville; John C. Tabone.
Bothell, all of Wash.; Gerald D. Hurst.
Iowa City, Iowa

[73] Assignee: EPOCH Pharmaceuticals, Inc.,
Bothell, Wash.

[21] Appl. No.: 334,490

[22] Filed: Nov. 4, 1994

Related U.S. Application Data

[63] Continuation of Ser. No. 49,807, Apr. 20, 1993, abandoned,
which is a continuation of Ser. No. 353,857, May 18, 1989,
abandoned, which is a continuation-in-part of Ser. No.
250,474, Sep. 28, 1988, abandoned.

[51] Int. Cl.⁶ C07H 19/04; C07H 21/00;
C07H 21/02; C07H 21/04

[52] U.S. Cl. 536/26.7; 536/24.5

[58] Field of Search 536/26.1, 26.12,
536/26.13, 26.14, 26.8, 27.6, 27.81, 28.5,
28.54, 26.7, 24.5

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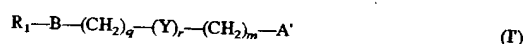
Primary Examiner—Gary L. Kunz

Attorney, Agent, or Firm—Klein & Szekeres, LLP

[57]

ABSTRACT

This invention is directed to novel substituted nucleotide bases with a crosslinking arm which accomplish crosslinking between specific sites on adjoining strands of oligonucleotides or oligodeoxynucleotides. The invention is also directed to oligonucleotides comprising at least one of these crosslinking agents and to the use of the resulting novel oligonucleotides for diagnostic and therapeutic purposes. The crosslinking agents of the invention are of the following formula (I):



wherein,

R₁ is hydrogen, or a sugar moiety or analog thereof optionally substituted at its 3' or its 5' position with a phosphorus derivative attached to the sugar moiety by an oxygen and including groups Q₁, Q₂ and Q₃ or with a reactive precursor thereof suitable for nucleotide bond formation;

Q₁ is hydroxy, phosphate or diphosphate;

Q₂ is =O or =S;

Q₃ is CH₂-R', S-R', O-R', or N-R'R";

each of R' and R" is independently hydrogen or C₁₋₆ alkyl;

B is a nucleic acid base or analog thereof that is a component of an oligonucleotide;

Y is a functional linking group;

each of m and q is independently 0 to 8, inclusive;

r is 0 or 1; and

A' is a leaving group.

This invention is also directed to novel 3,4-disubstituted and 3,4-trisubstituted pyrazolo[3,4-d]pyrimidines and to the use of these nucleic acid bases in the preparation of oligonucleotides. The invention includes nucleosides and mono- and oligonucleotides comprising at least one of these pyrazolopyrimidines, and to the use of the resulting novel oligonucleotides for diagnostic purposes.